REMARKS

Applicant requests reconsideration of the present application in view of the discussion that follows. The status of the claims is as follows. Claims 1-34 were pending. The Examiner has withdrawn claims 1-18 from consideration and such claims have been canceled herein without prejudice to Applicant's filing of divisional applications to the separately patentable subject matter thereof.

Objection to the Specification

The Examiner contends that the listing of references in the specification is not a proper information disclosure statement and that 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office. Further, the Examiner asserts that MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, states the Examiner, unless the references have been cited by the examiner on form PTO-892 or by applicant on form PTO-1449, they have not been considered.

As the Examiner has acknowledged, Applicant has submitted an Information Disclosure Statement (IDS) with a listing of references (Form PTO-1449). The references cited by Applicant are those considered by Applicant to be material to the patentability of the presently claimed invention. The Examiner indicated that this IDS was considered as to the merits before First Action.

In the objection, the Examiner specifically referred to page 12 of the present specification. On page 12, Applicant stated that exemplary signal-producing systems are described in U.S. Patent No. 5,508,178 (Rose, *et al.*), the relevant disclosure of which is incorporated herein by reference. The reference was cited in the present specification to provide general information to the skilled artisan concerning signal-producing systems. This reference was not cited in the IDS because of its general nature with respect to the presently claimed invention.

At the conclusion of the section of the Office Action entitled "OBJECTIONS MAINTAINED," the Examiner stated that "Applicants have not addressed the following objection. Accordingly it is maintained." Applicant interpreted this to refer to the prior paragraphs and that the statement more properly should have been placed after the title

of the section or after the heading "Information Disclosure Statement." If Applicant's interpretation is incorrect, Applicant respectfully requests that Applicant be given the opportunity to address this issue.

Previous Objection to the Specification

Applicant acknowledges that the Examiner has withdrawn the previous objection to the specification as to the Brief Description of the Drawings and as to the use of trademarks.

Previous Rejection under 35 U.S.C. §112

Applicant acknowledges the Examiner's withdrawal of the rejection of Claims 19-34 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Previous Rejection under 35 U.S.C. §103

Applicant acknowledges the Examiner's indication that the previous rejections as listed below have been withdrawn.

1) Claims 19-20 and 23-26 under 35 U.S.C. 103(a) as being unpatentable over Erb, *et al.* (U.S. Patent No. 6,251,688) (Erb 1) and Erb, *et al.* (U.S. Patent No. 6,300,082) (Erb 2) in view of Zhang, *et al.*, (The Journal of Biological Chemistry, 268 (14), May15, 1993, pages 10095-10101) (Zhang).

2) Claims 21 and 22 under 35 U.S.C. 103(a) as being unpatentable over Erb 1 and Erb 2 in view of Zhang and further in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

3) Claims 27-34 under 35 U.S.C. 103(a) as being unpatentable over Erb 1 and Erb 2 in view of Zhang and in further view of Zuk, *et al.* (U.S.Patent No. 4,281,061) (Zuk).

Discussion of Certain Aspects of the Invention

Applicant first would like to discuss certain aspects of the present invention prior to addressing the rejections in the Office Action in order to avoid any misunderstanding concerning aspects of the present methods.

As indicated in the present specification, high volume screening for drugs of abuse is currently carried out commercially by conducting a series of individual homogeneous immunoassays (EMIT or FPIA). A cut off level is set for each drug, which is used to establish whether a particular result will be defined as positive or negative. It is necessary for testing laboratories to handle separate reagent sets and carry out separate assays for each of the commonly abused drugs in every sample. Typically, the presence of as many as six drugs must be determined.

Among those homogeneous assays that have been used commercially or are particularly good candidates for drug screening, EMIT®, CEDIA®, FRAT® and SLFIA have the property of having an increase in signal with an increase in drug concentration. However, because of sensitivity problems or problems intrinsic to these methods, assays for low concentration analytes can have relatively high negative signals, sometimes more than 50% of the maximum possible signals. Combined assays, therefore, show a serious loss in sensitivity. Moreover, induced luminescence assays have decreased signals (fluorescence polarization and chemiluminescence, respectively) with increasing drug concentration and are, therefore, poor candidates for a combined drug assay.

The present invention permits effective screening of samples for the presence of one or more of a plurality of different analytes. For example, the present invention provides for screening a sample for one or more of a plurality of drugs of abuse where one is attempting to ascertain whether a sample contains any of the plurality of drugs. For example, one may be interested in determining whether a sample contains one or more of cocaine, marijuana, heroin, morphine and LSD. In accordance with the present invention, the sample to be tested is combined in a medium with an antibody for each of the drugs of interest. Accordingly, antibodies for each of cocaine, marijuana, heroin, morphine and LSD are added to the medium along with the sample. Also added to the medium, for each of the drugs, is a first reagent comprising (i) a first label, (ii) a small

molecule and (iii) a drug analog, wherein the drug analog competes with the drug, if present, for binding to the antibody for the drug. Thus, multiple first reagents are added to the medium, one each for each of cocaine, marijuana, heroin, morphine and LSD. Also added to the medium is a second reagent comprising (i) a second label and (ii) an antibody for the small molecule, wherein the first label and the second label interact in close proximity to produce a predetermined increased amount of signal if one or more of cocaine, marijuana, heroin, morphine and LSD are present in the sample. A single second reagent is added for all of the drug analytes of interest in the sample. The medium is examined for the amount of the signal, the predetermined increased amount thereof being related to the presence of one or more of cocaine, marijuana, heroin, morphine and LSD in the sample.

The methods of the invention are less expensive and faster than known methods because it is only necessary to carry out one assay per sample. The present invention avoids the difficulty of producing multiple independent signals. In the method of the invention, only one signal is produced in the assay. The intensity of the signal exceeds a certain threshold and indicates the presence, above its predetermined cut-off level, of one of the target analytes.

Rejection under 35 U.S.C. §102

Claims 19-20 and 23-26 were rejected under paragraph (b) of the above code section as being anticipated by Oh, *et al.* (U.S. Patent No. 5,851,778 and WO 89/03041) (collectively, Oh). The above disclosures are essentially duplicative and will be addressed herein collectively. In addressing the arguments of the Examiner below, Applicant is accepting, solely for the purpose of argument, the Examiner's assertion that the tridentate conjugate of Oh is equivalent to the first reagent of the present invention. In doing so, Applicant is not acquiescing in this interpretation.

In order to maintain a rejection under 35 U.S.C. §102(b), the Examiner must first establish a *prima facie* case of anticipation. An invention is anticipated if each and every limitation of the claimed invention is disclosed in a single prior art reference. *In re Paulsen*, 30 F.3d 1475, 1478, 31 U.S.P.Q.2d 1671, 1673 (Fed. Cir. 1994). In the present situation Oh does not disclose each and every element of the claimed invention.

For example, Oh fails to disclose or suggest an assay for the determination of one or more of a plurality of analytes of interest in a sample. Oh does not disclose or suggest adding multiple antibodies, one each for each of the suspected analytes. Oh fails to disclose or suggest adding multiple first reagents, one each for each of the suspected analytes. As can be seen, for example, from Oh's examples, the patentee assays for a single analyte. See, for example, column 37, lines 34-48. In the example, an aliquot of the patient's sample is combined with an aliquot of the tridentate solution. The combined solution is then incubated with the optimized antibody solution. Then, an aliquot of the optimized proximity label solution is added. After inclusion of the substrate solution, signal is measured. The patentee indicates that the same procedure is repeated for various dilutions of a theophylline or theophylline-amine standard. In this way a standard curve is obtained and the concentration of theophylline or theophylline-amine in the sample can be extrapolated.

Oh! not multiple analytes.

Rejection under 35 U.S.C. §103

Claims 21 and 22 were rejected under 35 U.S.C. 103(a) as being unpatentable over Oh in view of Maggio. In order to maintain a rejection under 35 U.S.C. §103 the Examiner must first establish a *prima facie* case of obviousness. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); *In re Piasecki*, 745 F.2d 1468, 223 U.S.P.Q. 785 (Fed. Cir. 1984). In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the references before him to make the proposed substitution, combination or other modification. *In re Lintner*, 458 F.2d 1013, 173 U.S.P.Q. 560 (C.C.P.A. 1972). In determining the scope and content of the prior art, references must be considered in their entirety, as a whole, including portions that would lead away from the claimed invention. *In re Panduit*, 810 F.2d 1561, 1 U.S.P.Q.2d 1593 (Fed Cir. 1987). Hindsight reconstruction using the disclosure and claims in prosecution as a guide to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention is not permitted. *In re Fine*, *supra*.

The Examiner argues that Oh differs from the instant invention in not specifically teaching the detection assay employing a solid phase such as particles. However, asserts the Examiner, Maggio discloses enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was mede to use solid phase/particles as taught by Maggio in the assay method to detect the drug interaction of Oh.

Oh is deficient as discussed above and Maggio does not cure these deficiencies.

Claims 27-34 were rejected under paragraph (a) of the above code section as being unpatentable over Oh in view of Zuk, *et ál.* (U.S. Patent No. 4,281,061) (Zuk). The Examiner recognizes that Oh fails to teach a kit. However, asserts the Examiner, Zuk teaches kits and it would have been obvious to one skilled in the art at the time of the invention to formulate the assay of Oh into a kit.

Oh is deficient as discussed above and Zuk does not cure these deficiencies.

Hindsight

Applicant submits that, in order for one to modify the deficient teachings of the reference to achieve the methods of the present invention, one would have to use Applicant's disclosure because the references do not teach anything relevant to the screening assay as claimed. As has been held, there must be some suggestion, motivation or teaching in the prior art whereby the person of ordinary skill would have selected the components that the inventor selected and used to make the new invention (*C.R. Bard, Inc. v M3 Systems, Inc.*, 157 F.3d 1340, 48 U.S.P.Q.2d 1225 (Fed. Cir. 1998), *cert. denied*, 67 U.S.L.W. 3715 (1999)).

Applicant further submits that, even if the fanciful combination of the teachings of the references were made, one still would not be in possession of the presently claimed invention. As explained above, none of the references discloses or suggests the reagents employed by Applicant in the present methods. None of the references discloses of suggests, either individually or in combination, a simultaneous determination of the presence of one or more drugs suspected of being present in a sample using the reagents as set forth in the claims.

Conclusion

Claims 19-34 satisfy the requirements of 35 U.S.C. §§102 and 103. Allowance of the above-identified patent application, it is respectfully submitted, is in order.

In any event, Applicant requests entry of the above amendment because it narrows the number of issues and places the application in better form for consideration on appeal.

Respectfully submitted,

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